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## **Abstract**

**Objective:** Longitudinal research into early intervention for youth at ultra high risk (UHR) for psychosis demonstrates beneficial outcomes including increased treatment compliance and greater participation in education and the workforce. Despite known barriers for rural youth accessing mental health services, research comparing urban and rural UHR youth is lacking. The study included an examination of the impact of substance use on functioning of UHR youth. **Method:** Youth aged 12-25 years were recruited from the urban area of Newcastle or the rural area of Orange, New South Wales, Australia, and identified as UHR by the Comprehensive Assessment of At Risk Mental States (CAARMS). Rural and urban youth were compared on clinical profiles, social and occupational functioning, and substance use. **Results:** The rural youth showed different help seeking behaviours and had greater functional impairment than urban youth. Substance use was common across the sample of 57 youth (mean age 16.5 years, 56% female) and a history of hazardous substance use was associated with higher levels of depression. Rural youth ( $n=32$ ) were more likely than urban youth to be taking antidepressants at baseline (44% compared to 16%). **Conclusion:** Different patterns of help seeking by rural UHR youth suggest a need for greater access to psychosis informed primary care early intervention services. Interventions should target functional decline to prevent adverse outcomes such as reduced community participation and unemployment. In addition, interventions for substance use should

be a priority for UHR youth, who should also be screened and monitored for depressive symptoms and treated for depression if indicated.

**Keywords**

Ultra high risk, psychosis, rural, youth, substance use

**Running head**

Rurality and psychosis risk

Clinical Trial: This study was registered with the Australian New Zealand Clinical Trials

Registry number ACTRN 12606000101583.

## **Background**

There is substantial geographical variability in the burden of ill-health between metropolitan and rural regions in many countries (1, 2). For example, Australian and international reports have found poorer physical health, increased socio-economic disadvantage, and poorer access to health and social services in rural and remote areas (3). In particular, Australian rural youth (18-24 years) experience lower social support and are significantly more likely than urban youth to consume alcohol at hazardous levels (up to 37% of rural youth), and have significantly higher rates of death by injury (up to 5 times their urban counterparts) or suicide (4). A significant decline in functioning in adolescence occurs for young people at risk of developing psychosis or with a first episode of psychosis (FEP; 5) and reduced participation in school, vocational training or employment is an important risk factor for social exclusion (6, 7). Despite the health inequalities of rural residency, there is a lack of research examining the clinical and functioning profiles of young rural people at risk for developing psychosis.

In recent decades there have been assertive attempts to identify individuals at ultra high risk (UHR) of developing psychotic disorders. Three common criteria are often used within UHR samples, identifying individuals with a recent decline in functioning along with either genetic vulnerability, attenuated positive symptoms and/or frank intermittent psychotic symptoms (8). Assessment for UHR is usually conducted using a

semi-structured clinical interview such as the Comprehensive Assessment of At Risk Mental States (CAARMS; 8). No known studies have investigated differences in presentation and outcomes of rural versus urban youth deemed at UHR of psychosis.

Despite our knowledge of the challenges faced by rural youth such as reduced access to services and limited social support, there is a paucity of research into the management and outcomes of early psychosis in rural areas. An Australian survey of mental health service directors found that rural and remote public mental health services showed the lowest levels of early psychosis intervention implementation (9). The few published studies of early psychosis intervention in rural settings tend to describe service models rather than provide clinical information about the youth attending the services (10). As a result, little is known about rural youth at UHR of psychosis. Youth from rural and urban areas often have different demographic characteristics, and rural youth have reduced access to specialist mental health services, and greater distances to travel to reach services (10, 11). These factors present possible barriers to early identification of UHR youth in the rural environment. Therefore, it is timely to consider the similarities and differences between rural and urban youth deemed at UHR of psychosis.

Adolescents in rural Australia have been shown to be at greater risk of alcohol use than urban youth (12) and substance use is associated with poor health outcomes for those experiencing a first episode of psychosis (13). In the UHR population, higher levels of

substance use are associated with more severe symptoms (14). Specifically, a dose-response relationship between heavy cannabis use and transition to psychosis in UHR individuals was reported by a meta-analysis (15). Recent research has shown UHR individuals to have significantly higher rates of tobacco, alcohol and cannabis use than help seeking non-UHR individuals (16).

The current study aimed to compare the demographic characteristics, substance use patterns, functioning and clinical presentations of rural and urban youth identified at UHR of psychosis. In addition, the study sought to examine the impact of substance use on functioning of UHR youth. The data were drawn from the baseline assessments of the DEPTH trial (17), a single blind randomised controlled trial comparing the effectiveness of cognitive behaviour therapy (CBT) and non-directive reflective listening (NDRL) in ameliorating 'at risk mental states' for psychosis and delaying or preventing transition to psychosis among UHR youth recruited from urban and rural locations.

## **Method**

### *Participants*

Youth aged 12 – 25 years were recruited in the urban Newcastle region and the rural Orange region of New South Wales (NSW), Australia. For the urban site, youth were primarily recruited through the Psychological Assistance Service (PAS), an early psychosis clinical service established in 1997 with a focus on identification and

treatment of young people at risk of psychosis (18, 19) (20). The rural site was located at the Centre for Rural and Remote Mental Health, a research unit of the University of Newcastle in the central west region of rural NSW. This site did not have access to a specialised early psychosis service and hence relied upon promotion of the research within health and non-health services to facilitate recruitment. Youth were eligible for the study if they: (i) were aged 12-25 years; (ii) resided within the Newcastle region of the Hunter New England Area Health Service (urban sample) or within a 170km radius (for accessibility for weekly therapy) of Orange in the Greater Western Area Health Service (rural sample); and (iii) met criteria for one or more of three 'at risk mental states' as defined by the Comprehensive Assessment of at Risk Mental States (CAARMS; 8). Recruitment for the rural and urban samples is illustrated in Figure 1. Youth were excluded from the study if they: (i) met criteria for a past or current DSM-IV-TR psychotic disorder; (ii) had previously been prescribed anti-psychotic medication at a therapeutic level (considered a sign of transition); (iii) had an organic mental disorder or intellectual disability; (iv) were at serious suicidal or homicidal risk (they were eligible for inclusion once this risk was resolved); or (v) had an inadequate command of the English language (due to the verbal demands of therapy and assessment). The study was approved by the Human Research Ethics Committees of the participating institutions.

INSERT FIGURE 1 HERE

## *Procedure*

Participants meeting eligibility criteria for the DEPT<sub>H</sub> trial completed a baseline assessment. This assessment involved completing a series of clinical interviews with a registered psychologist with extensive experience providing assessment and treatment for UHR and FEP youth. Participants completed a range of reliable and valid measures, each widely used within clinical samples. In addition to demographic information, the following measures were completed at baseline.

### *Mental health measures*

*The Comprehensive Assessment of At-Risk Mental States* (CAARMS; 8) is a semi-structured interview used to determine whether individuals meet criteria for being at UHR of psychosis. There are three UHR groups defined by the CAARMS: (i) Group A - trait and state risk factor (Trait) (genetic vulnerability due to having a schizotypal personality disorder, or a first-degree relative with a psychotic disorder); (ii) Group B - attenuated psychotic symptoms (APS) (sub-threshold, attenuated positive psychotic symptoms); and (iii) Group C - brief limited intermittent psychotic symptoms (BLIPS) (short episodes of frank psychotic symptoms that have resolved without treatment); with each group including chronic low or a significant decrease in functioning.

The *Structured Clinical Interview for DSM-IV – Clinical Version* (SCID-CV: 21) is a semi-structured interview that systematically assesses whether individuals meet diagnostic criteria for DSM-IV Axis I diagnoses.



The *Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version* (K-SADS-PL: 22) is a semi-structured interview based on DSM-III-R and DSM-IV criteria, designed to assess current and previous episodes of psychopathology in children and adolescents. The K-SADS-PL was substituted for the SCID-CV to assess diagnoses for any participant younger than 18 years.

The *Brief Symptom Inventory* (BSI: 23) is a self-report inventory in which individuals report the extent to which they have experienced a range of symptoms in the past week. The individual items contribute to nine subscales: somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobia, paranoia, and psychoticism. In addition, the measure provides a Global Severity Index and a Positive Symptom Distress Index.

#### *Substance use measures*

The *Opiate Treatment Index* (OTI: 24) is a structured interview that systematically assesses the individual's use of substances. For each substance, a Q-score is calculated that provides an estimate of the average number of use occasions per day during the past month. Hazardous substance use was defined as at least weekly use of any illicit drug or drinking 2 or more (females) or 4 or more (males) standard drinks a day.

The *Alcohol Use Disorders Identification Test* (AUDIT: 25, 26) is a 10-item assessment used to assess an individual's level of consumption and problems associated with alcohol use. A total score greater than 8 is indicative of likely hazardous or harmful

alcohol use in adults, while a cut-score of 3 or 4 is suggested for adolescents. The AUDIT was administered as an interview within the current study.

The *Cannabis Use Disorders Identification Test – Revised* (CUDIT-R: 27) is an 8-item screener used to assess an individual's cannabis use. A total score greater than 13 is indicative of likely presence of a current cannabis use disorder. The CUDIT-R was administered as an interview within the current study.

#### *Role function and well-being measures*

The *Global Assessment of Functioning* (GAF: 28) is a clinician-rated measure of social, occupational, and psychological functioning. Ratings are made on a scale from 0 to 100, with high scores indicative of higher levels of global functioning.

The *Social and Occupational Functioning Assessment Scale* (SOFAS: 29) is a clinician-rated measure of social and occupational functioning. Ratings are made on a scale from 0 to 100, with high scores indicative of higher levels of functioning.

The *Rosenberg Self-Esteem Scale* (30) is a 10-item self-report measure. Each item is rated on a 4-point Likert-type response scale, with high total scores associated with greater self-esteem.

The *Quality of Life Scale* (QLS: 31) is a 21-item semi-structured interview. Domains assessed include interpersonal relations, instrumental role functioning, intrapsychic

foundations, and common objects and activities. Each item is rated on a 7-point anchor system, with low scores associated with poorer quality of life.

#### *Data analysis*

Data were analysed using IBM SPSS statistical software (Version 22.0; Armonk, NY, USA). Two sets of comparisons are reported, based on recruitment location (urban vs. rural) and substance use history (no history vs. hazardous use); these two variables were relatively independent in the current sample (hazardous substance use history: urban, 40.0%; rural, 31.3%,  $p = 0.492$ ). For the categorical outcome variables, simple  $\chi^2$  tests were used, while independent samples t-tests were used for the continuous outcome variables. The threshold for statistical significance was set at  $p < 0.05$ .

### **Results**

#### *Combined sample*

The demographic characteristics, CAARMS UHR criteria, and DSM diagnostic clusters within the sample are reported in Table 1.

INSERT TABLE 1 HERE

Three of the 60 youth who completed the assessment and randomisation subsequently declined to participate in the study. The final sample of 57 youth was predominantly female (58%) with a mean age of 16.5 years (range 12-25 years). The majority were still living in the family home (77%) and studying full time (56%). Around

10% of the youth were engaged in casual or part-time employment while 19% reported being unemployed. There were no significant differences between the rural and urban samples on any of these demographic characteristics. Consistent with other UHR studies, the majority of youth met UHR criteria on the CAARMS for attenuated symptoms (81%) while 33% met familial risk criteria, and only 7% met the Brief Limited Intermittent Psychotic Symptom (BLIPS) criteria. The most commonly occurring DSM-IV diagnoses in both urban and rural groups tended to be depressive (Major Depressive Disorder) and anxiety disorders.

*Rural and urban youth*

Whilst rural and urban youth were very similar on many variables, including gender, age, clinical symptoms, and CAARMS profiles, there were significant differences in previous contacts with care providers. A greater proportion of urban youth reported previous contacts with school counsellors and general practitioners than rural youth. Conversely, a greater proportion of rural youth were prescribed antidepressant medication (40.6%) compared to urban youth (16.0%).

INSERT TABLE 2 HERE

As shown in Table 2, functional impairment was significantly greater for rural than urban youth across most domains of measurement. Rural youth were more impaired than urban youth in role and social functioning as well as overall quality of life and

global functioning. Overall, one third of the sample reported current alcohol and tobacco use.

#### *Substance use history*

Those with a history of hazardous substance use ( $n=20$ ) were significantly older than those without such a history ( $n=37$ ) and also reported worse depressive symptoms on the BSI; however, these subgroups tended to have similar diagnostic, mental health contacts, and social and global functioning profiles (see Tables 1 and 2). It is noteworthy that those with a history of hazardous substance use also had mean levels of alcohol use that fell within the *risky or hazardous* alcohol use level for adults on the AUDIT. Although there were no significant differences between urban and rural youth, the mean AUDIT score for the rural youth reached the cut-score for adolescents of 4.

#### **Discussion**

The current study aimed to compare the demographic characteristics, substance use patterns, and clinical presentations of rural and urban youth identified at UHR of psychosis. While there were no significant differences in demographic characteristics, UHR clinical presentations as defined by the CAARMS, or substance use, rural UHR youth differed from urban youth in patterns of help seeking, and prescribed medications as well as social and role functioning.

Help-seeking behaviour was significantly different between rural and urban youth, with rural youth more likely to have sought help from community mental health services rather than primary health care. Urban youth predominantly accessed primary care services as has been shown in other UHR studies (32). This pattern was also reflected in referral sources such that rural youth were more likely than urban youth to have been referred to the trial by mental health services. These findings suggest there are differences in the types of care providers and treatment approaches available to rural youth. The greater reliance on tertiary mental health services by rural UHR youth in our trial may have arisen from lower intake thresholds for rural compared to urban community mental health services. A more likely explanation might be related to the limited availability of primary care in rural areas (33). In these circumstances, youth might have delayed accessing assistance for emergent mental health symptoms until they were acutely unwell and required tertiary care.

In addition, the availability of specialist early psychosis services differed between the rural and urban recruitment sites. In the rural recruitment area there was no existing specialist early psychosis service. The DEPT<sub>H</sub> trial presented the rural community mental health team with an opportunity for their clients to access specialist early psychosis assessment and intervention. In contrast, the urban recruitment site occurred within an established early psychosis clinical service, and the high rate of referrals from general practitioners likely reflected existing clinical referral pathways.

Despite there being no differences in diagnoses, with the predominant diagnoses for both rural and urban youth being mood or anxiety disorders, rural youth were significantly more likely to have been prescribed antidepressant medication than urban youth. This higher level of prescribing antidepressants may be related to the scarcity of allied health practitioners and non-government organisations within rural areas (11). The Outreach and Support in South London (OASIS) service showed that 14% of UHR youth were prescribed antidepressants prior to accessing the service(34). While the OASIS study found the prescribing of antidepressants was associated with higher rates of depressive comorbidities in the sample, this was not the case for our sample.

Functional impairment was significantly greater for rural than urban youth across all domains of measurement in our trial. This included social and role functioning thus indicating a negative impact on school and employment. Not surprisingly, then, the rural youth reported poorer quality of life than urban youth. Our previous research examining the impact of prolonged drought on the social context for a community sample of rural youth showed increasing levels of psychological distress associated with declines in social networks due to relocation of families out of the drought affected area(35). While impaired social and occupational functioning (30% drop in past 12 months) is a criterion for UHR status, the average level of functional impairment for our sample is consistent with other studies (36, 37). Impaired social functioning has been shown to be predictive of transition to psychosis (38) and

impairment in UHR similar to that of FEP (39). As such, the greater social functioning decline in our rural, compared to urban, youth may indicate more proximal risk for transition to psychosis.

This functional impairment is likely to have adverse outcomes into adulthood such as reduced community participation, employment and social inclusion. For our sample, this functional impairment of UHR rural youth may reflect delayed access to services given there were no differences in diagnostic profiles compared to urban UHR youth. A recent systematic review found that negative and disorganised symptoms and neurocognitive impairment are key drivers of functional impairment in the UHR population (40). This could be explored further in future research examining how negative symptoms or neurocognitive impairment may contribute to differences in functional impairment between rural and urban UHR youth. Compromised social functioning will impact on relationships with peers and family, engagement in education, and negotiation of help seeking for health and vocational needs (41). Compromised social functioning may also reduce opportunities for exploring alternative explanations for unusual thoughts and anomalous perceptual experiences (42). As such, early intervention services for rural youth could be enhanced by increasing the awareness by clinicians of UHR profiles and using the early psychosis model for early intervention service delivery (11) with a focus on improving functioning (40).



Tobacco and other substance use was reasonably common in both rural and urban youth. Although not significant, the mean AUDIT score for the rural sample was higher, reaching the cut-off for problematic alcohol consumption among adolescents. A history of hazardous substance use was associated with higher levels of depression. Recently, Barrowclough and colleagues reported that heavier alcohol use was associated with higher levels of depression among an established psychosis sample (43). Similarly tobacco smoking has been associated with depression and cessation with improved mood (44). Thus, interventions for substance use among UHR urban and rural young people UHR should be a priority and should include screening and counselling to reduce tobacco, alcohol, cannabis and other drug use and depressive symptoms.

### **Strengths and limitations**

Consistent with other studies of UHR youth (39), there were difficulties recruiting to the trial with 25% fewer participants than planned and thus the trial was underpowered. While the trial utilised a robust design with an active control condition, the small sample may have reduced the ability to detect group differences. The analysis allowed for an examination of the impact of factors such as comorbid disorders on functioning but contextual factors such as socioeconomic status or social isolation were not examined in the dataset.

### **Conclusion**

Different patterns of help seeking by rural UHR youth indicate a need for greater access to psychosis informed primary care services, which is critical to prevent impaired functioning and reduced quality of life. Importantly, interventions should target functional decline to prevent adverse outcomes such as reduced community participation and unemployment. In addition, interventions for tobacco, alcohol, cannabis and other substance use should be a priority for UHR youth, who should also be screened and monitored for depressive symptoms and treated for depression if indicated. Further research is warranted to explore early intervention models to enhance access to care for rural UHR youth and to explore the mechanisms for the greater functional impairment of rural UHR youth.

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**Table 1.** Socio-demographic and diagnostic comparisons based on location and substance use history for ultra high risk youth (N=57)

Characteristic	Location				Substance Use History		<i>p</i>
	Urban ( <i>n</i> =25)	Rural ( <i>n</i> =32)	Combined ( <i>n</i> =57)	( <i>Urban vs. Rura</i> ) <i>p</i>	No history ( <i>n</i> =37)	Hazardous Use ( <i>n</i> =20)	
Gender - % Female	64.0%	56.3%	57.9%		62.2%	55.0%	
Mean age (s.d.)	17.2 (3.03)	15.87 (2.76)	16.46 (2.93)		15.84 (2.63)	17.60 (3.17)	*
Current Status							
Working	16.0%	9.4%	12.3%		10.8%	15.0%	
Studying	60.0%	65.6%	63.1%		67.6%	55.0%	
Neither	24.0%	25.0%	24.6%		21.6%	30.0%	
Past Mental Health Contact							
School counsellor	48.0%	18.8%	31.6%	*	32.4%	30.0%	
General practitioner	60.0%	25.0%	40.4%	**	40.5%	40.0%	
Mental health professional	48.0%	62.5%	56.1%		64.9%	40.0%	
Other	24.0%	31.3%	28.1%		21.6%	40.0%	
CAARMS UHR Criteria							
Familial	28.0%	37.5%	33.3%		35.1%	30.0%	
Attenuated	72.0%	87.5%	80.7%		78.4%	85.0%	
BLIPS	3.1%	12.0%	7.0%		8.1%	5.0%	
Diagnostic cluster (SCID / K-SADS)							
Depression	40.0%	28.1%	33.3%		32.4%	35.0%	
Anxiety	40.0%	28.1%	33.3%		35.1%	30.0%	
Substance abuse	16.0%	6.3%	10.5%		0.0%	30.0%	n/a
Behavioural problem	12.0%	15.6%	14.0%		16.2%	10.0%	
Antidepressant medication	16.0%	40.6%	29.8%	*	29.7%	30.0%	

CAARMS: Comprehensive Assessment of At Risk Mental States; SCID: Structured Clinical Interview for DSM Axis I Disorders; K-SADS: Kiddie-Schedule for Affective Disorders and Schizophrenia. Statistical comparisons:  $\chi^2$  for categorical variables, and t-tests for continuous variables.

\**p*<.05; \*\**p*<.01; n/a for variables associated with sub-group definitions.

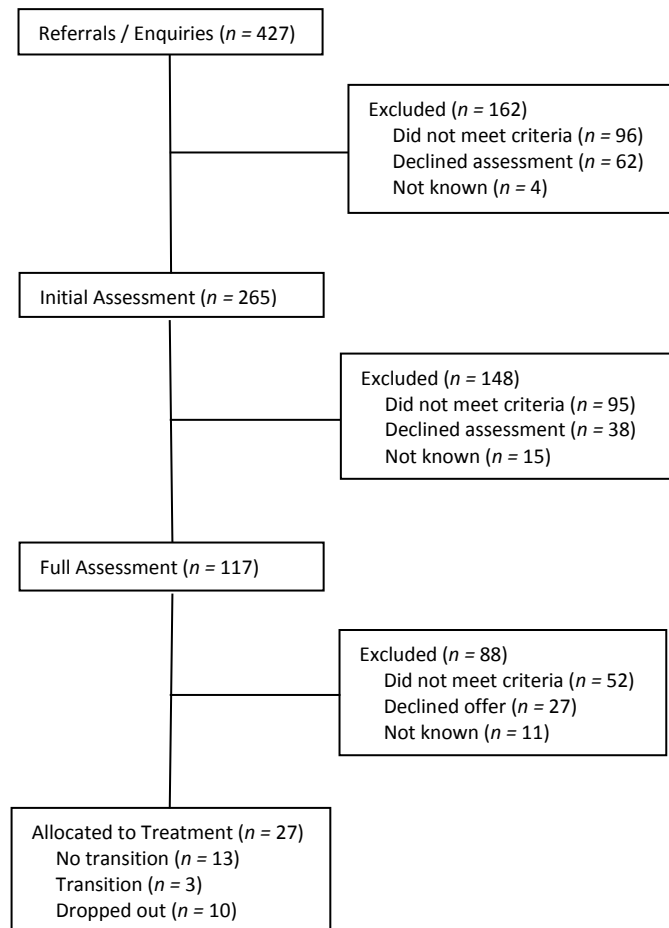


**Table 2.** Current functioning comparisons based on location and substance use history for ultra high risk youth (N=57)

Current Functioning	Location			Substance Use History		
	Urban (n=25)	Rural (n=32)	<i>p</i>	No history (n=37)	Hazardous Use (n=20)	<i>p</i>
Current Substance Use						
OTI – Tobacco	2.89 (6.75) [8.68]	3.07 (6.26) [7.92]		1.45 (5.23) [7.68]	6.15 (7.56) [8.52]	n/a
OTI – Alcohol	0.63 (1.59) [1.89]	0.92 (3.03) [2.60]		0.07 (0.31) [0.44]	2.28 (4.00) [3.16]	n/a
OTI – Cannabis	0.00 (0.01) [0.04]	0.82 (3.69) [12.67]		0.00 (0.00)	1.41 (4.81) [8.46]	n/a
OTI – Polydrug Score	0.75 (0.99)	0.87 (0.99)		0.35 (0.59)	1.78 (0.94)	n/a
AUDIT	1.96 (5.70)	4.37 (8.25)		0.68 (1.73)	8.61 (10.74)	n/a
CUDIT-R	0.73 (3.41)	1.26 (4.30)		0.00 (0.00)	3.44 (6.68)	n/a
Self-Esteem Scale	26.00 (1.00)	22.34 (4.85)		23.13 (4.40)	21.56 (5.64)	
Quality of Life Scale	85.57 (19.51)	64.81 (23.91)	***	71.94 (24.17)	77.06 (24.80)	
BSI Subscales						
Depression	1.41 (1.45)	1.96 (1.09)		1.57 (1.06)	2.39 (1.29)	*
Global Severity Index	1.34 (1.00)	1.65 (0.82)		1.51 (0.85)	1.73 (0.91)	
Social and Occupational Functioning Assessment Scale	60.95 (11.22)	50.14 (9.20)	***	55.15 (12.59)	53.28 (8.70)	
Global Assessment of Function	58.47 (10.77)	50.07 (8.71)	***	53.66 (10.40)	52.41 (10.36)	

OTI: Opiate Treatment Index, values in square brackets show mean usage by users; AUDIT: Alcohol Use Disorders Identification Test; CUDIT-R: Cannabis Use Disorders Identification Test – Revised; BSI: Brief Symptom Inventory. Statistical comparisons:  $\chi^2$  for categorical variables, and t-tests for continuous variables. \* $p<.05$ ; \*\* $p<.01$ , \*\*\* $p<.001$ ; n/a for variables associated with sub-group definitions.

### Urban Site: Newcastle



**Figure 1.** DEPTH trial recruitment at the urban and rural sites.

## Rural Site: Orange

